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GROUP 1600

RESPONSE UNDER 37 C.F.R. 1.116  
EXPEDITED PROCEDURE  
EXAMINING GROUP 1634

OFFICIAL

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S/N 09/125,953

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	FODSTAD et al.	Examiner:	Sisson, B.
Serial No.:	09/125,953	Group Art Unit:	1634
Filed:	December 10, 1998	Docket No.:	7885.56USWO
Title:	IMMUNO-MAGNETIC CELL SEPARATION USED IN IDENTIFICATION OF GENES ASSOCIATED WITH SITE-PREFERENCED CANCER METASTASIS FORMATION		

CERTIFICATE UNDER 37 CFR 1.6: The undersigned hereby certifies that this correspondence is being transmitted via facsimile to: TC1600, Commissioner for Patents, Washington, D.C. 20231 on July 26, 2002.

By:

Name: Nancy J. Parsons

AMENDMENT UNDER 37 C.F.R. § 1.116

Box AF  
Commissioner for Patents  
Washington, D.C. 20231

VIA FACSIMILE  
**TC1600**  
**703-872-9307**

Dear Sir:

In response to the Office Action mailed February 27, 2002, please consider the following amendments and remarks to this application.

In the Claims

Please cancel claim 5 and amend claims 2, 6 and 9 as follows:

- F<sub>1</sub>
2. (Twice Amended) Method according to claim 12, wherein the first and second tissue target cells are malignant cells obtained from solid primary or recurrent tumors, from metastases from such tumors to lymph nodes, blood, bone marrow, blood tissue, liver, lungs, central nervous system, malignant pleural effusions and ascites, urine, cerebral spinal fluid, or other organ sites.
- F<sub>2</sub>
6. (Twice Amended) Method according to claim 12, further comprising the step of cloning RNA and DNA extracted from the isolated cells.
- F<sub>3</sub>
9. (Twice Amended) Method according to claim 8, wherein the expression pattern of identified gene sequences from two or more tumor sites are compared.

### Remarks

This is in response to the final Office Action mailed February 27, 2002. Claim 5 has been canceled and claims 2, 6 and 9 have been amended. The amendments to the claims are supported in the specification as filed. No new matter has been added. Applicants respectfully request entry of the above amendment. Attached herewith is an unsigned declaration by the inventor under 35 U.S.C. §1.132. A signed copy will be forwarded to the Examiner as soon as possible.

#### Rejections under 35 U.S.C. §112, first paragraph

Claims 2, 3, 5-9 and 12 remain rejected as not enabled by the specification. The Examiner asserts that the specification does not provide reaction conditions, and that the situation is analogous to that in *Genentech v. Novo Nordisk*. Applicants respectfully traverse the rejection. In the amendment and response filed November 5, 2001, Applicants provided a detailed discussion and examples showing that the state of the art relating to the individual method steps recited in the instant claims, at the time the application was filed, was such that the skilled artisan would know how to perform those individual method steps. See pages 3-6 of the previous response. In the final Office Action, the Examiner failed to address any of these arguments, and has simply maintained the rejection.

Applicants hereby request the Examiner respond to the arguments presented in the previous response. Additionally, MPEP 2164.01 cites several cases in support of the fact that a patent need not teach, and preferably omits, what is well known in the art. Regarding undue experimentation, MPEP 2164.01(a) states that factors to be considered include: breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The Examiner has not addressed any of these factors. The Examiner has merely stated that since no specific reaction conditions are listed in the specification, the specification does not enable the claims.

In further support of the enablement of the invention, Applicants hereby submit a declaration under 37 CFR §1.132 by the inventor. The enclosed declaration provides evidence of the state of the art at the time the invention was made. As stated in the previous response, the specification provides references as examples of some of the many different ways of performing the individual method steps required in the claimed methods. Applicants submit that the level of skill in the areas of cell isolation and mRNA analysis at the time the invention was made was such that, upon reading the instant specification, one would have been able to practice the invention. Withdrawal of the rejection is respectfully requested. If this rejection is maintained, Applicants respectfully request the Examiner address all of the previous arguments presented in the response of November 5, 2001, and additionally, provide an indication of how the factors set forth in MPEP 2164.01(a) were considered with respect to the area of art related to the claims.

Regarding claim 2, Applicants are unsure how the claim has been interpreted as reciting the simultaneous screening of 12 or more different samples. However, in the interest of advancing prosecution, claim 2 has been amended. Claim 2 clearly recites a listing of different tissues from which the first and second tissues recited in claim 12 could be taken. Applicants submit that claim 2 is fully supported and enabled by the specification as filed. Withdrawal of the rejection is respectfully requested.

Claims 2, 3, 7-9 and 12 remain rejected as having sufficient breadth of scope so to encompass conducting the assay either *in vivo* or *in situ*. Claim 5 has been incorporated in amended claim 6. The claims, as amended, are directed to analyzing nucleic acids extracted from the isolated cells. Withdrawal of the rejection is respectfully requested.

Claim 9 remains rejected as not enabled by the disclosure as it relates to studying the pattern of expression for the "identified genes". The Examiner asserts that the disclosure does not set forth a repeatable procedure whereby any gene has actually been identified and studied. Page 5, starting with line 6, provides this disclosure. The specification teaches using known gene cloning procedures, such as those taught by a cited reference, to analyze and compare the genes expressed in a first population of tumor cells with the genes expressed in other cells. Example 1, starting on page 5, line 35, provides a specific example of the method of claim 9. Primary breast tumor cells, tumor

cells from lymph nodes, bone marrow cells, and peripheral blood cells were collected, RNA was extracted, and partial cDNA was obtained and compared on sequencing gels. The specification specifically teaches "we have found one cell cycle related transcription factor, one oncogene product" at page 6, lines 18-19. Additionally, Example 2 on pages 6 and 7 teaches the discovery of two genes using the claimed method, LV1 and LV12, that are differentially expressed in MA-11 human breast cancer cells.

The Examiner asserted that no indication had been provided of which prior art teachings would fully enable the claimed method of claim 9. Applicants submit that the specification clearly sets forth such teachings, for example the Liang and Pardee reference cited on page 5, line 8. The Examiner also argues that Applicants' previous argument, that the successes of the claimed method were not contemplated prior to the filing of the present application, conflicts with the assertion of enablement. The claimed method is directed to identifying genes differently expressed between cells isolated from different tissue. This is what had not been contemplated prior to the present application. This method requires performing multiple steps that had not previously been combined to achieve the results of identifying differently expressed genes. While the individual method steps, i.e. immunomagnetically isolating cells, determining mRNA levels in cells, and comparing levels of mRNA, are known to the skilled artisan, the specific combination of steps claimed had not been contemplated prior to the instant invention. Applicants submit that claim 9 is fully supported and enabled by the specification as filed. Withdrawal of the rejection is respectfully requested.

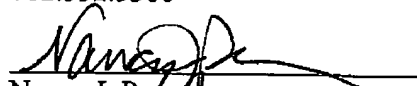
#### Conclusion

In view of the amendments, declaration and comments presented herein, favorable reconsideration in the form of a Notice of Allowance is respectfully requested.

Respectfully submitted,

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